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Lymphography in Childhood: Six Years Experience with 242 Cases

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Summary

From January, 1969 – December, 1974, 242 children less than 15 years of age underwent lymphography at the National Cancer Institute, Milan. Successful lymphatic cannulation was accomplished in 97% (440/463) of the sites where it was attempted. No major or permanent complications were encountered, although minor untoward effects might not have been recorded. In those children undergoing biopsy of opacified lymph nodes, lymphographic-histologic correlation was 98% (45/46).

Nonspecific reactive hyperplasia lymphographic patterns were encountered in 36% of all studies, confirming its high incidence in the pediatric age group.

This study has shown that lymphography in childhood can be as readily performed as in the adult and that its diagnostic accuracy is acceptable. As in adults, it is useful in treatment planning, evaluating results of therapy, and detecting recurrent tumor. The frequent occurrence of nonspecific reactive hyperplasia in the pediatric lymphogram should not be mistaken for evidence of tumor, particularly lymphoma.

Introduction

Lymphography is an established diagnostic procedure in the clinical investigations of a variety of malignant diseases. Although lymphography was employed in the pediatric age group early in the clinical experience with this technique (1), there are surprisingly few reports concerning pediatric lymphographic experience with large groups of patients (5, 7,.8, 9, 10).

Opponents of lymphography have claimed that it is technically difficult to perform and to interpret, that it is attended by significant complications, and that it is of questionable reliability. These presumed drawbacks are generally assumed to be greater in the pediatric age group. We therefore report the recent experience with 242 consecutive children in whom lymphography was performed.

Materials and Methods

As determined from the records of the Radiology Department and Pediatric Oncology Division, there were 242 children less than 15 years of age who underwent lymphography at the National Cancer Institute, Milan, Italy, during the 6 year period of January 1969 – December 1974. Some of these studies were included in prior reports covering different time periods and utilizing different interpretative criteria (9, 10). All pertinent radiographs relative to the lymphogram were reviewed for each case by two diagnostic radiologistis (R.C., R.M.), who were provided with no clinical information except for the histologic or presumed type of tumor for which the study was requested. Repeat lymphograms were not analyzed for this report.

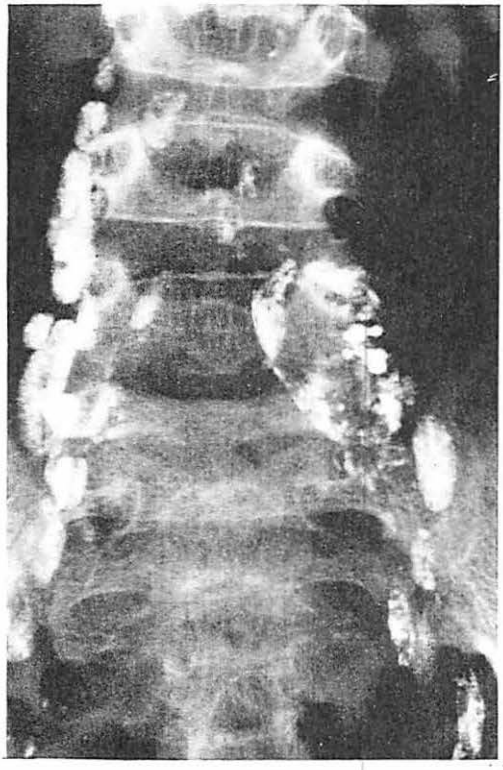

Fig. 1 *Neuroblastoma, bladder base,* in a 9 year old girl. A single, enlarged left common iliac lymph node with large filling defects was interpreted as a metastasis (biopsy confirmed). Lymphatic deviation was seen on the initial films.

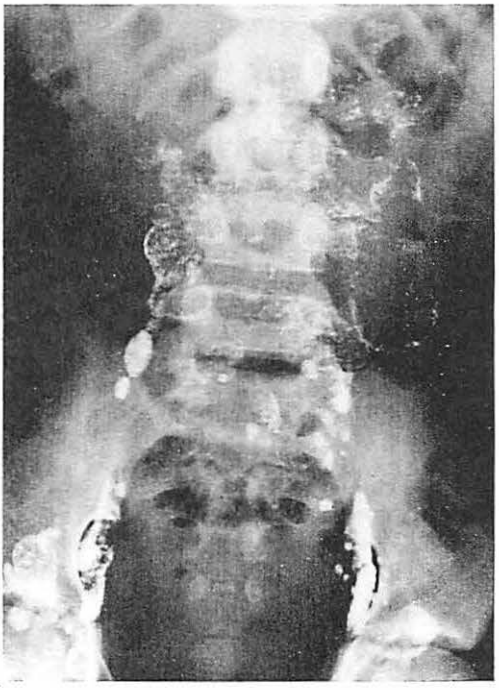

Fig. 2 *Hodgkin's Disease,* nodular sclerosing, in a six year old boy. Multiple enlarged, foamy lymph nodes, particularly in the paralumbar region were seen (biopsy confirmed).

The lymphograms were interepreted as being: 1) normal; 2) abnormal due to benign changes, i.e., hyperplasia; or 3) abnormal due to underlying disease, i.e., positive studies. No equivocal diagnostic category was employed (2, 12). Strict criteria were used in formulating the lymphographic diagnosis. In brief, discrete filling defects with lymphatic deviation or obstruction were required for a diagnosis of metastasis from an epithelial tumor (Fig. 1). Enlarged, foamy lymph nodes with multiple, ill-defined, filling defects were interpreted as compatible with Hodgkin's disease or non-Hodgkin's lymphoma (Fig. 2). The lymphographic diagnosis of non-specific reactive (follicular) hyperplasia was based on diffusely enlarged and prominently granular lymph nodes (a "magnification radiography" effect) (2, 3, 12) at all sites or in those chains draining lower extremity tumors (Fig. 3).

The lymphographic interpretation was then correlated with other clinical data, including results of biopsies of opacified lymph nodes. It was also noted whether the lymphogram was performed as part of the initial evaluation of a newly diagnosed patient prior to any therapy, except for the surgical excision of a mass from which the diagnosis was first made ("previously untreated" group); or whether it was performed following some therapy ("previously treated" group).

The technique of performing the lymphogram in the pediatric age group was the same as in the adult, including utilization of the same surgical instruments and cannulating needles (27-30 gauge). Likewise, the ability to identify, isolate, and cannulate the lymphatic in a child was similar to the adult. (With few exceptions, all lymphograms in this report were performed by R.M.). The amount of iodized oil (Lipiodol) injected was considerably less than in the adult, and studies were carefully monitored to provide an optimum study with a minimum of oily contrast media. Over the course of this study, the amount of contrast media decreased so that at present the infusion of contrast is terminated when channels are opacified at the level of the L_5-S_1 interspace. Thus, optimal studies could be obtained with as little as 1-1.5 cc total Lipiodol.

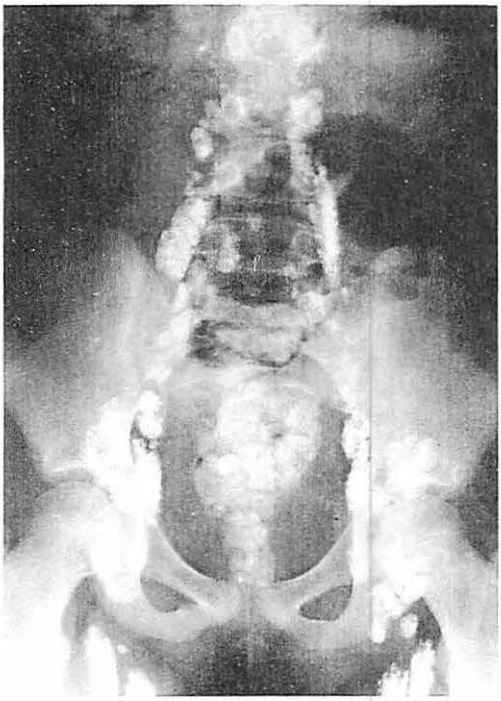

Fig. 3 *Reactive follicular hyperplasia,* in a 9 year old girl with a left Wilm's tumor. All lymph nodes are bulky in size and granular in internal archetecture (biopsy confirmed).

All children in this study received pre-operative sedation; furthermore, those children less than 10 years of age routinely received general anaesthesia, as did those older children who appeared unduly apprehensive or uncooperative. The standard anaesthetic approach, as employed at this institution, has been previously described (10) and is summarized in Table I. Endotracheal intubation has rarely been necessary and when employed was associated with large mediastinal or intraabdominal masses which impeded the child's breathing. More recently, Ketamine (Ketalas) has been used for pediatric lymphography. At a dose of 3 mg/Kg I.V. this drug provides a rapid general anaesthesia which can be maintained with repeat doses of 1.0-1.5 mg/Kg, without associated respiratory depression or vomiting. This method of anaesthesia is not completely satisfactory due to the possibility of undue movements. For this reason the use of Ketamine has been adopted as a preoperative sedation (2-4 mg/Kg I.M.) in association with an antisecretory drug such as Scopolamine.

Table 1 Anaesthesia in Pediatric Lymphography

Age (yrs)	Drugs and dosages	
	Pre-operative sedation	
0 – 3	Scopolamine	0.12-0.25 mg I.M.
	Thiobarbituric*	250 mg rectal suppository
4 – 10	Scopolamine	0.25 mg I.M.
	Perfenazine**	2.5-5.0 mg I.M.
11 – 15	Same as age 4 – 10 plus	
	Diazepam***	5 – 10 mg I.M.
	General anaesthesia	
0 – 15	Nitrous oxide	4 – 6 l/m
	Oxygen	2 – 3 l/m
	Fluothane	0.5 – 2% (Fluotic Mark II)
	or	
	Ethrane	1 – 4% (Enflurate, Abbott)

* Thiopentone ** Trilafon *** Valium

Results

Of the 242 children, there were 142 boys (59%) and 100 girls (41%), whose median age was 9.6 years (range 0.75-14.9 years of age). (Fig. 4) Eighty-three percent (200/242) were previously untreated children with newly diagnosed disease.

Lymphography via cannulation of a dorsal foot lymphatic was attempted in 241 patients (a 3 year old boy with a testicular tumor underwent a successful funicular lymphography). A sucessful bilateral lymphogram was obtained in 200 of the 211 children in whom this was attempted. A unilateral study was obtained in 9 children and in 2 children no lymphatic could be cannulated bilaterally. In the remaining 30 children a unilateral lymphogram was desired only on the side of a malignant tumor of the ipsilateral lower extremity, and in each case it was successfully accomplished. Thus, a successful lymphatic cannulation was accomplished in 97% (440/453) of the sites attempted.

No allergic-type reactions were encountered due to the local or general anaesthetic, vital blue dye, or iodized oil (Lipiodol), although minor manifestations such as itching and sneezing may have been obscured by the general anaesthetic when employed. No local wound infections or lymphangitis were encountered that were of sufficient concern to prompt a physician visit and

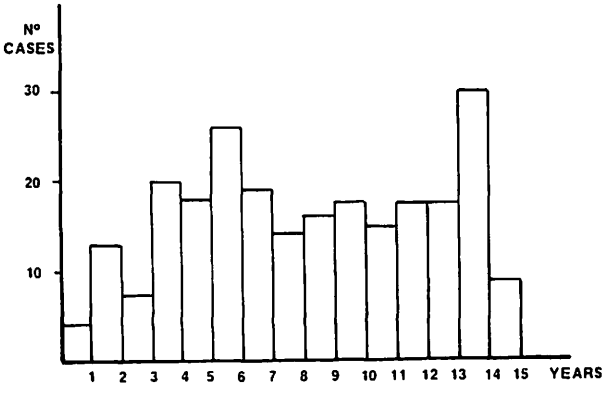

Fig. 4 Age distribution of children undergoing lymphography at the National Cancer Institute, Milan, from Jan 1969-Dec 1974.

Table 2 Results of Lymphography in Hodgkin's Disease

Clinical Stage	Number of cases	Positive
I	17*	0
II	27*	5
III_S	2	0
IV	2	2
Previously treated	12	6

* 2 cases with subdiaphragmatic onset.

Table 3 Results of Lymphography in non-Hodgkin's Lymphomas

Clinical Stage	Number of cases	Positive Lymphograms
I	3	0
I_E	4	0
II	10*	2
II_E	3	0
III	4	2
IV	16	8
Previously treated	13	2

*2 cases with subdiaphragmatic onset

thus appear in the medical records. Pulmonary embolization of Lipiodol could be detected, if searched for diligently, on most chest radiographs the following day, However, its occurrence was most commonly associated with no apparent change in the patient's pre-lymphographic status, as judged by the medical records. Minor complaints, such as coughing, low grade fever, or a difficult – to – evaluate symptom such as minimal dyspnea in a child, may not have been brought to the physician's attention. No radiographically detectable cases of hepatic or renal embolization were seen. In summary, no serious or distressing complications were encountered in the group of 242 children related to the performance of the lymphogram.

Hodgkin's Disease and non-Hodgkin's Lymphoma (Tables 2 and 3)

The largest group of children studied by lymphography had a malignant lymphoma and they comprise 47% (113/240) of evaluable cases.

There were 60 children with Hodgkin's disease, of which 48 were previously untreated. The lymphogram was positive in 50% of the 12 children who were previously treated, as compared to a 15% incidence of positive studies in the 48 previously untreated group. Of the 42 previously untreated children with supradiaphragmatic stage I or II disease at presentation, the lymphogram increased the stage of disease in 9% (4/42) of patients. The incidence of positive lymphograms relative to the histologic sub-type of disease was 6% (1/16) for lymphocyte predominace, 15% (2/13) for nodular sclerosis, 11% (1/9) for mixed cellularity, and 30% (3/10) for lymphocyte depletion in the previously intreated cases.

There were 53 children with non-Hodgkin's lymphoma, of which 40 were previously untreated. The lymphogram was positive in 30% of this previously untreated group, as compared to a 15% incidence of positive studies in the 13 previously treated children. Of the 18 previously untreated patients with stage I or II supradiaphragmatic disease, the lymphogram was positive in 1, and thus changed the stage in only 6% of cases.

Neuroblastoma (Table 4)

This was the most common solid tumor studied, and it accounted for 15% (36/240, excluding a 3 year old with neuroblastoma in whom the study was unsuccessful bilaterally) of all children undergoing lymphography. The overall incidence of positive lymphograms in this group was 47% (53% of previously untreated cases and 33% of previously treated cases); and the largest incidence occurred in those children with previously untreated intraabdominal tumor (15/24 = 61%). When positive the lymphograms usually demonstrated extensive involvement of the opacified lymph nodes (Fig. 5); at times, however, only a single lymph nodes was involved with tumor (Fig. 1).

Primary Bone Tumors

All 22 children with primary bone tumors of the lower extremity or pelvis who underwent lymphography were previously untreated. There were 3 positive lymphograms in this group,

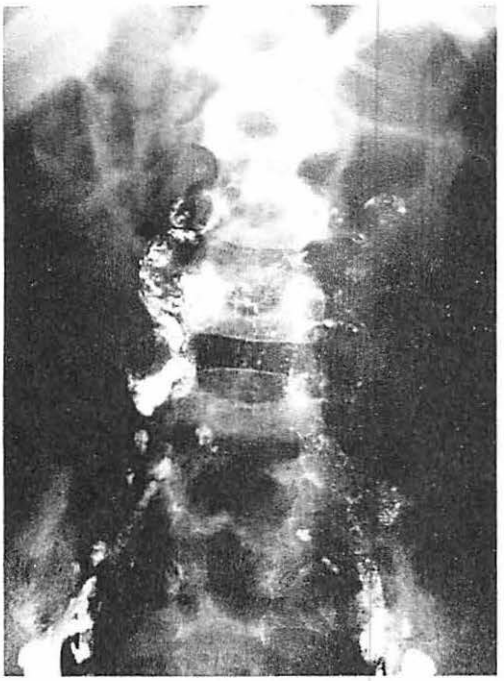

Fig. 5 *Neuroblastoma,* in a 4 year old boy. Typical appearance of a positive lymphogram caused by metastatic neuroblastoma, with marked involvement of the paralumbar lymph nodes extending into the iliac region (biopsy confirmed).

Fig. 6 *Ewing's sarcoma,* left fibula, in a 4 year old boy. An enlarged left inguinal lymph node containing a prominent filling defect which caused lymphatic deviation on the initial films was interpreted as a metastasis (biopsy confirmed). The more cephalad iliac and paralumbar nodes showed only a prominently granular pattern with some increase in size suggesting reactive hyperplasia (biopsy confirmed).

and each occurred in a child with a Ewing's sarcoma (Fig. 6). This tumor comprised 64% (14/22) of the cases in this group and had a 21% (3/14) incidence of lymph node metastases. There were no positive studies in the remaining 8 tumors (4 osteosarcomas, 2 chondrosarcomas, 1 histiocytosis X and 1 aneurysmal bone cyst with a preoperative X-ray diagnosis of sarcoma).

Wilms' tumor

Positive lymphograms were seen in 10% (2/20) of the 20 children in this group. Whereas no positive studies were seen in the 9 children who were investigated at the time of initial diagnosis, 18% (2/11) of the children studied during the course of their illness had lymphographic evidence of lymph node metastases.

Table 4 Results of Lymphography in Neuroblastoma

	Site of Origin	Number of cases	Positive Lymphograms
Previously Untreated	Abdomen	24	15
	Throax	1	0
	Unknown	5	1
Previously Treated	Abdomen	3	1
	Thorax	2	1
	Unknown	1	0
Totals		36	18

Gonadal tumors (Table 5)

Of the 12 children in this group (7 testicular and 5 ovarian tumors), 58% (7/12) had posi-

tive lymphograms. Seventy-one percent (5/7) of the lymphograms of the testicular tumors were positive compared to a 40% (2/5) incidence in ovarian neoplasms.

Table 5 Results of Lymphography in Gonadal Tumors

Site	Histologic Sub-type	Number of cases	Positive Lymphograms
Testis	Embryonal carcinomas	2	2
	Teratocarcinomas	2	2
Testis	Seminoma	1	1
	Fibrosarcoma	1	0
	Mesothelioma	1	0
		7	5
Ovary	Dysgerminoma	3	2
	Teratocarcinoma	1	0
	Teratoma	1	0
		5	2

Soft Tissue Sarcomas

Three of 10 children (30%) with soft tissue sarcomas of the lower extremity or abdomen had positive lymphograms (excluding a 9 year old in whom the study was unsuccessful bilaterally). Lymph node metastases were seen in 3 of 6 children with rhabdomyosarcoma, whereas all 4 with malignant mesenchymomas had normal studies.

Miscellaneous Malignant Tumors (Table 6)

The overall incidence of positive lymphograms in this group of 17 children with uncommonly encountered malignant tumors was 23% (4/17).

Table 6 Results of Lymphography in Miscellaneous Malignant Tumors

Tumor	Number of cases	Positive Lymphograms
Nasopharyngeal cancer	4	1
Melanoma (lower extremity)	3	1
Hepatocarcinoma	2	0
Bladder, rhabdomyosarcoma	2	0
Hypernephroma	1	1
Thymoma	1	0
Endodermal sinus tumor	1	0
Mesenteric sarcoma	1	0
Medullary malignant hystiocytosis	2	1
Totals	17	4

Miscellaneous non-Malignant Diseases

There were 10 children in whom a malignant disease was never proven. Five children were studied because of a clinical suspicion of lymphoma and all had normal studies. The remaining 5 children had tuberculosis (2 cases), sarcoidosis, lymphedema of presumed congenital origin, and a lymphangioma of the lower leg. Abnormal lymphograms, compatible with the underlying disease were seen in one child with tuberculosis and in the child with lymphangioma (Fig. 7).

Lymphographic-Histologic Correlation (Table 7)

In 46 children lymph nodes opacified on the lymphogram were surgically excised, either in the course of staging the tumor (e.g. lymphoma), or as part of the therapeutic approach (e.g. testicular neoplasms).

There was agreement between the lymphographic interpretation and the histologic finding in the biopsied lymph nodes in 98% (45/46) of cases. The single lymphographic error was a falsely-negative diagnosis.

Fig. 7 *Lymphangioma,* right lower leg, in a nine year old girl (biopsy proven). Note the multiple, punctate collections of contrast material within the edematous soft tissues posteriorly and medially, presumably representing opacification of the dilated lymphatic spaces within the tumor. Although there was considerable perivascular extravasation, no evidence of lymphatic obstruction such as dermal backflow was seen.

Table 7 Radiographic-Histologic correlation

Tumor	Number of patients with lymph node biopsy	Lymphography / Histology			
		+/+	+/-	-/+	-/-
Hodgkin's disease	25	7	-	-	18
Non-Hodgkin's lymphoma	8	1	-	1	6
Ewing's sarcoma	2	2	-	-	-
Testis carcinoma	4	4	-	-	-
Rhabdomyosarcoma	2	1	-	-	1
Malignant mesenchymoma	1	-	-	-	1
Wilm's tumor	1	-	-	-	1
Melanoma	1	1	-	-	-
Nasopharyngeal cancer	1	1	-	-	-
Clinical suspicion of lymphoma	1	-	-	-	1
Totals	46	17	-	1	28

Non-specific Reactive Hyperplasia (Figures 3 and 6)

The overall incidence of non-specific reactive hyperplasia encountered in the various groups was 36% (86/240), with a range of 20-86%. The occurrence of non-specific reactive hyperplasia was particularly high in the groups with primary bone tumors (82%) and in miscellaneous non-malignant diseases (70%).

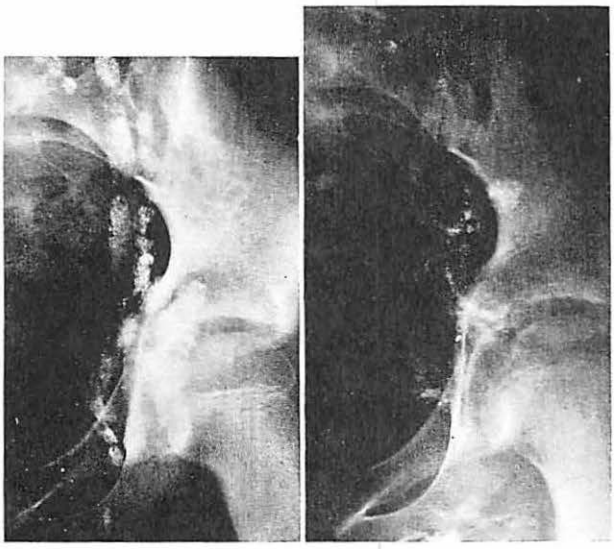

Fig. 8 *Ewing's sarcoma relapse,* detected on surveillance follow-up in a 9 year old girl; (Left) The lymphogram was interpreted as being negative. (Right) Three months later, a repeat radiograph showed interval marked enlargement of many external iliac lymph nodes, interpreted as representing relapse.

This report overlaps with prior studies from this institution which concerned pediatric lymphography at different time periods (9, 10). More importantly, this report utilized different criteria for interpreting the lymphogram which is based upon increasing experience with lymphographic-histologic correlation from material obtained at "staging" or therapeutic lymph node biopsies (2, 4, 11, 12, 13, 14).

The experience with lymphography at the National Cancer Institute in Milan is extensive, so that the pediatric lymphograms presented in this report represent 7.3% (242/3308) of the patient so examined over this 6 year period. This large experience undoubtedly contributed to the high success rate of lymphatic cannulation of 97%. It should be remembered that in cases in which a bilaterally attempted study is only successful on one side, the unilaterally opacified iliac, and bilaterally opacified para-aortic, lymph nodes usually provide substantial diagnostic information. Thus in only 0.83% (2/242) was the study completely non-productive.

In approximately 1/5 of children the accuracy of the lymphographic interpretation could be determined based upon appropriate lymph node biopsies. The high accuracy of 98% must be viewed with some caution, since the children undergoing biopsy represent a selected sub-group which might well introduce a favourable bias. Also, this is a retrospective study and the lymphographic interpretations were made by radiologists specifically interested and experienced in lymphography. Nevertheless, certainly the accuracy of lymphography in the pediatric age group can be expected to be at least as good as in the adult experience (2, 4, 6, 8, 11, 12, 13, 14). And, as in the adult, periodic surveillance abdominal films will at times indicate the appearance of tumor activity (Fig. 8).

This study confirms the frequent occurrence of non-specific reactive hyperplasia patterns encountered on the pediatric lymphogram. Since it usually is a diffuse and symmetric process, it is readily recognized as an unimportant variation. However, it is important not to confuse these reactive, enlarged, prominently granular lymph nodes as nodes containing tumor, particularly lymphoma (3).

The frequent use of general anaesthesia to perform the lymphogram (approximately 70% of cases) in this institution is based on several premises. It was found to be convenient to perform several diagnostic procedures at one time (such as lymphography, arteriography, bone marrow

biopsy, etc.) utilizing the same anaesthesia. It was also felt that general anaesthesia provided optimal working conditions for the radiologist which resulted in a more rapid and safer study. Furthermore, for the child general anaesthesia provides a study free of anxiety and pain associated with the diagnostic radiologist and X-ray department. Thus the child does not view with apprehension or fear each of the many subsequent visits he will make during the course of his illness.

A retrospective review of the medical record to obtain data regarding the incidence of complications related to the lymphogram will almost certainly underestimate the magnitude of this problem. We are therefore not able to provide strong data on this point. As noted, we found no instance of a potential complication to be of sufficent concern to prompt a specific note in the medical record. Although no serious complications were encountered in this group of children, this study can not specifically address this important area.

This study has shown that lymphography in the pediatric age group can be as readily performed as in the adult and that its diagnostic accuracy should be at least as good as in the older age group. Likewise, it is useful in treatment planning, in evaluating the results of therapy, and detecting recurrent tumor. The frequent occurrence of non specific reactive hyperplasia in the pediatric lymphogram should not be mistaken for evidence of tumor, particularly lymphoma.

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